BPR1J-097 Hydrochloride

Cat. No.: HY-13537A

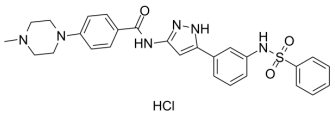
Molecular Formula: $C_{27}H_{29}ClN_6O_3S$

Molecular Weight: 553.08

Target: FLT3

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 6 mg/mL (10.85 mM; Need ultrasonic and warming)
H_2O : 2 mg/mL (3.62 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.8081 mL	9.0403 mL	18.0806 mL
	5 mM	0.3616 mL	1.8081 mL	3.6161 mL
	10 mM	0.1808 mL	0.9040 mL	1.8081 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

BPR1J-097 Hydrochloride is a novel and potent FLT3 inhibitor with an IC_{50} of 11 nM.

IC_{50} & Target

IC50: 11 nM (FLT3)[1]

In Vitro

BPR1J-097 Hydrochloride is a novel and potent FLT3 inhibitor with an IC_{50} of 11nM. Phosphorylation of all FLT3-WT, FLT3-IDT, and FLT3-D835Y are inhibited by BPR1J-097 Hydrochloride at a concentration as low as 10 nM. BPR1J-097 Hydrochloride suppresses the phosphorylation of FLT3 and STAT5 in a dose-dependent manner. The IC_{50} values of BPR1J-097 Hydrochloride on MOLM-13 and MV4-11 cells are 21±7 and 46±14 nM, respectively. The emergence of active caspase-3 is observed in MOLM-13 cells treated with BPR1J-097 Hydrochloride at 10 nM. The effect of BPR1J-097 Hydrochloride seems to be weaker in MV4-11 cells as caspase-3 is not evident until 100 nM of BPR1J-097 Hydrochloride is applied to treat cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

After i.v. administration of mice with BPR1J-097 Hydrochloride at two cycles of 10 or 25 mg/kg, a clear dose-dependent anti-tumour effect is observed. Tumours in mice treated with BPR1J-097 Hydrochloride (25 mg/kg per day) stop growing. BPR1J-097 Hydrochloride (25 mg/kg) shows a significant tumour shrinkage effect on the subcutaneously growing MOLM-13 tumours in a size of >2000 mm^3. BPR1J-097 Hydrochloride (10 and 25 mg/kg) also produces a dose-dependent growth

	reduction and shrinkage of another model using MV4-11 cells. It is noted that a prolonged disappearance of MV4-11 tumours is observed in mice treated with BPR1J-097 Hydrochloride at 25 mg/kg. There is little (3%) or no body weight loss of BPR1J-097 Hydrochloride-treated nude mice during the observation periods in these in vivo studies[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The FLT3 Kinase-Glo kinase assays are carried out in 96-well plates at 30°C for 4 h in a final volume of 50 µL, including 25 mM Tris pH 7.4, 10 mM $MgCl_2$, 4 mM $MnCl_2$, 1 mM DTT, 0.02% Triton X-100, 0.01% BSA, 1 µM ATP, 20 µM peptide (GGMEDIYFEFMGGKKK), 75 ng recombinant FLT3 proteins, and test compound (BPR1J-097) at the indicated concentration. After incubation, 50 µL Kinase-Glo Plus Reagent is added and incubated at 25°C for 20 min. A 70 µL aliquot of each reaction mixture is transferred to a black microtiter plate and the luminescence is measured on a multilabel counter. Each IC_{50} value is determined by three different experiments[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Proliferation assays are performed by seeding 10 000 cells per well in a 96-well culture plate. After 16 h, cells are then treated with vehicle or BPR1J-097 Hydrochloride at various concentrations in medium for 72 h. Cell viability is quantitated using the MTS method. The results are determined by measuring absorbance at 490 nm using a plate reader. The GC_{50} value is defined as the amount of compound that causes 50% reduction in cell viability in comparison with DMSO-treated (vehicle) control and is calculated using Prism version 4 software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male nude mice of 8 weeks of age are used. Nude mice (n=5 to 7 per group) are inoculated subcutaneously with MOLM-13 (1×10^6 per flank) or MV4-11 cells (5×10^6 per flank). When the tumour size reaches 100 to 200 mm^3, animals are grouped and treated with BPR1J-097 Hydrochloride at various doses in a 2-week treatment period as indicated. Animals are treated with BPR1J-097 Hydrochloride (10 and 25 mg/kg, i.v.) or vehicle as control at once daily for 5 days per week for 2 weeks. Tumour volumes are measured and calculated with the formula length×$width^2/2$ after initiation of treatments. Tumour size and animal body weight are measured twice a week after tumour cell inoculation. At the end of the study, animals are killed by carbon dioxide inhalation followed by cervical dislocation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lin WH, et al. BPR1J-097, a novel FLT3 kinase inhibitor, exerts potent inhibitory activity against AML. Br J Cancer. 2012 Jan 31;106(3):475-81.

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